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| Substitute for form 1449A/B/PTO |   |    |   | Complete if Known      |                           |
|                                 |   |    |   | Application Number     | NEW- 10/517,450           |
|                                 |   |    |   | Filing Date            | December 9, 2004          |
|                                 |   |    |   | First Named Inventor   | Marc DONATH               |
|                                 |   |    |   | Art Unit               | NIA 1647                  |
|                                 |   |    |   | Examiner Name          | Not Yet Assigned Ian Dang |
| Sheet                           | 1 | of | 1 | Attorney Docket Number | 4614-0160PUS1             |

| U.S. PATENT DOCUMENTS |                       |  |                  |   |   |
|-----------------------|-----------------------|--|------------------|---|---|
| Examiner Initials*    | Cite No. <sup>1</sup> | Document Number                          | Publication Date | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|                       |                       | Number-Kind Code <sup>2</sup> (if known) | MM-DD-YYYY       |   |   |
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| FOREIGN PATENT DOCUMENTS |                       |   |                                |   |   |
|--------------------------|-----------------------|---|--------------------------------|---|---|
| Examiner Initials*       | Cite No. <sup>1</sup> | Foreign Patent Document   | Publication Date<br>MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|                          |                       | Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known) |                                |   |   |
| /I.D./BA                 | EP-1 018 514-A        |   | 07-12-2000                     |   |   |

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| NON PATENT LITERATURE DOCUMENTS |                       |  |  |  |  |
|---------------------------------|-----------------------|--|--|--|--|
| Examiner Initials*              | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.                        |  |  |  |
| /I.D./                          | CA**                  | Dinarello et al., "Blocking IL-1: interleukin 1 receptor antagonist in vivo and in vitro", Immunology Today, Vol. 12, No. 11, 1991, pages 404-410.   |  |  |  |
|                                 | CB**                  | Mandrup-Poulsen et al., "Involvement of interleukin 1 and interleukin 1 antagonist in pancreatic and beta-cell destruction in insulin-dependent diabetes mellitus", Cytokine, Vol. 5, No. 3, 1993, pages 185-191.  |  |  |  |
|                                 | CC**                  | Meier et al., "IL-1 receptor antagonist serum levels are increased in human obesity: a possible link to the resistance to leptin?", Journal of Clinical Endocrinology & Metabolism, Vol. 87, No. 3, 2002, pages 1184-1188.   |  |  |  |
|                                 | CD**                  | Donath et al., "Hyperglycemia-induced beta-cell apoptosis in pancreatic islets of Psammomys obesus during development of diabetes", Diabetes, Vol. 48, No. 4, 1999, pages 738-744.   |  |  |  |
|                                 | CE**                  | Bedoya et al., "Pyrrolidine dithiocarbamate prevents IL-1-induced nitric oxide synthase mRNA, but not superoxide dismutase mRNA, in insulin producing cells", Biochemical and Biophysical Research Communications, Academic Press Inc., Florida, Vol. 210, No. 3, 1995, pages 816-822. |  |  |  |
|                                 | CF**                  | Yamamoto et al., "Role of the NF-kappaB pathway in the pathogenesis of human disease states", Current Molecular Medicine, Bentham Science Publishers, Great Britain, Vol. 1, No. 3, 2001, pages 287-296.   |  |  |  |
|                                 | CG**                  | Flodstroem et al., "Cytokines activate the nuclear factor KAPPAB (NF-KAPPAB) and inducenitric oxide production in human pancreatic islets", FEBS Letters, Elsevier Science Publishers, The Netherlands, Vol. 385, No. 1/2, 1996, pages 4-6.  |  |  |  |
| ↓                               | CH**                  | Maedler et al., "Glucose-induced beta cell production of IL-1beta contributes to glucotoxicity in human pancreatic islets", Journal of Clinical Investigation, Vol. 110, No. 6, 2002, pages 851-860.   |  |  |  |

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. \*\* CITE NO.: Those document(s) which are marked with an double asterisk (\*\*) next to the Cite No. are not supplied because they were previously cited by or submitted to the Office in a prior application relied upon in this application for an earlier filing date under 35 U.S.C. 120.

<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached.

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| Examiner Signature | /ian Dang/ | Date Considered | 03/27/2007 |
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**INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION**

(Use several sheets if necessary)

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## APPLICANT

DONATH, Marc

Examiner: Ian Dang

## FILING DATE

December 9, 2004

## GROUP

Art Unit 1647

## U. S. PATENT DOCUMENTS

| EXAMINER INITIAL | DOCUMENT NUMBER | Kind | DATE | NAME | CLASS | SUB CLASS | FILING DATE<br>IF APPROPRIATE |
|------------------|-----------------|------|------|------|-------|-----------|-------------------------------|
|                  | US              |      |      |      |       |           |                               |

## FOREIGN PATENT DOCUMENTS

|       | Office | DOCUMENT NUMBER | Kind | DATE | COUNTRY | CLASS | SUB CLASS | TRANSLATION |    |
|-------|--------|-----------------|------|------|---------|-------|-----------|-------------|----|
|       |        |                 |      |      |         |       |           | YES         | NO |
| I.D./ | EP     | 1018514A1       |      | 7/00 | EPO     |       |           |             |    |
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**OTHER DOCUMENTS** (Include Name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.)

|       |   |
|-------|---|
| I.D./ | Blocking IL-1: Interleukin 1 receptor antagonist in vivo and in vitro, Charles A. Dinarello, et al., <i>Immunology Today</i> , Vol. 12 No. 11 199, pp. 404-410  |
|       | Involvement of Interleukin 1 and Interleukin 1 Antagonist in Pancreatic B-Cell Destruction in Insulin-Dependent Diabetes Mellitus, Thomas Mandrup-Poulsen, et al., <i>Cytokine</i> , Vol. 5, No. 3 (May), 1993 pp. 185-191  |
|       | IL-1 Receptor Antagonist Serum Levels Are Increased in Human Obesity: A Possible Link to the Resistance to Leptin?, Christoph A. Meier, et al., <i>The Journal of Clinical Endocrinology &amp; Metabolism</i> 87(3):1184-1188                                     |
|       | Hyperglucemia-Induced B-Cell Apoptosis in Pancreatic Islets of Psammomys obesus During Development of Diabetes, Marc Y. Donath, et al., <i>Diabetes</i> , Vol. 48 April 1999, 738-744   |
|       | Pyrrolidine Dithiocarbamate Prevents IL-1-Induced Nitric Oxide Synthase mRNA, but not Superoxide Dismutase mRNA, in Insulin Producing Cells, F.J. Bedoyua, et al., <i>Biochemical and Biophysical Research Communications</i> , Vol. 210, No. 3 1995, pp. 816-822 |
|       | Role of the NF- $\kappa$ B Pathway in the Pathogenesis of Human Disease States, Yumi Yamamoto and Richard Gaynor, <i>Current Molecular Medicine</i> 2001, 1, pp. 287-296  |
|       | Cyokines Activate the Nuclear Factor $\kappa$ B (NF- $\kappa$ B) and Induce Nitric Oxide Production in Human Pancreatic Islets, Maline Flodström, et al., <i>Federation of European Biochemical Societies</i> 285 (1996) 4-6                                      |
|       | Glucose-induced B cell Production of IL-1B contributes to Glucotoxicity in Human Pancreatic Islets, Kathrin Maedler, et al., <i>The Journal of Clinical Investigation</i> , Sept. 2002, Vol. 110, Number 6, pp. 851-860   |
|       | Hyperglycaemia as an Inducer as well as a Consequence of Impaired Islet Cell Function and Insulin Resistance: Implications for the Management of Diabetes, R.H. Under, et al., <i>Diabetologia</i> , (1985) 28: 119-121   |
|       | Monolayer Culture of Adult Rat Pancreatic Islets on Extracellular Matrix: Modulation of B-Cell Function by Chronic Exposure to High Glucose, Nurit Kaiser, et al., <i>Endocrinology</i> , Vol. 129, No. 4, pp. 2067-2075  |
|       | Chronic Hyperglycemia Is Associated with Impaired Glucose Influence on Insulin Secretion, A Study in Normal Rats Using Chronic In Vivo Glucose Infusions, L. J. Leahy, et al., <i>J. Clinical Invest.</i> , Vol. 77 March 1986, pp. 908-915                       |
|       | Perspective in Diabetes, Type II Diabetes, Glucose "Non-Sense," and Islet Desensitization, R. Paul Robertson, <i>Diabetes</i> , Vol. 38, December 1989, pp. 1501-1505   |
|       | Glucose Toxicity, Luciano Rossetti, M.D., et al., <i>Diabetes Care</i> , Vol 13, No. 6, June 1990, pp. 610-630  |

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|----------|------------|-----------------|------------|
| EXAMINER | /Ian Dang/ | DATE CONSIDERED | 03/27/2007 |
|----------|------------|-----------------|------------|

I.D./

Prolonged Exposure of Human Pancreatic Islets to High Glucose Concentrations in Vitro Impairs the B-Cell Function, Decio L. Elizirik, *J. Clin. Invest.*, Vol. 90, October 1992, pp. 1263-1268

Impaired B-Cell Functions Induced by Chronic Exposure of Cultured Human Pancreatic Islets to High Glucose, Sonya Marchak, et al., *Diabetes*, Vol. 48m June 1999, pp. 1230-1236

Glucose Induces B-Cell Apoptosis Via Upregulation of The Fas Receptor in Human Islets, Kathrin Maedler, et al., *Diabetes*, Vol. 50, August 2001, pp. 1683-1690

High Glucose Causes Apoptosis in Cultured Human Pancreatic Islets of Langerhans, A Potential Role for Regulation of Specific Bcl Family Genes Toward an Apoptotic Cell Death Program, Massimo Federici, et al., *Diabetes*, Vol. 50, June 2001, pp. 1290-1301

Glucose and Tolbutamide Induce Apoptosis in Pancreatic B-Cells, Ioulia B. Efanova, et al., *The Journal of Biological Chemistry*, Vol. 273, No. 50, Issue of December 11, pp.33501-33507

Distinct Effects of Saturated and Monounsaturated Fatty Acids on B-Cell Turnover and Function, K. Maedler, et al., *Diabetes*, Vol. 50, January 2001, pp. 69-76

Long Term Effects of Aminoguanidine on Insulin Release and Biosynthesis: Evidence That the Formation of Advanced Glycosylation End Products Inhibits B Cell Function, Yuji Tajiri, et al., *Endocrinology*, Vol. 138, No. 1, pp. 273-280

Preservation of Insulin mRNA Levels and Insulin Secretion in HIT Cells by Avoidance of Chronic Exposures to High Glucose Concentrations, R. Paul Robertson, *J. Clin. Invest.*, Vol. 90, August 1992, pp. 320-325

Differentiating Glucose Toxicity From Glucose Desensitization: A New Message From the Insulin Gene, R. Paul Robertson, et al., *Diabetes Center and the Division of Diabetes, University of Minnesota Medical School*

The Role of Interleukin-1 in the Pathogenesis of IDDM, T. Mandrup-Poulsen, *Diabetologia* (1996) 39: pp. 1005-1029

Cytokines Cause Functional and Structural Damage to Isolated Islets of Langerhans, T. Mandrup-Poulsen, et al., *Allergy* 1985, 40, pp. 424-429

Cytotoxicity of Human pI 7 Interleukin-1 for Pancreatic Islets of Langerhans, Klaus Bendtzen, et al., *Science*, Vol. 232, pp. 1545-1547

Interleukin 1 Dose-Dependently Affects the Biosynthesis of (pro) Insulin in Isolated Rat Islets of Langerhans, G.A Spinas, et al., *Diabetologia*, (1987) 30: pp. 474-480

Affinity-Purified Human Interleukin I is Cytotoxic to Isolated Islets of Langerhans, T. Mandrup-Poulsen, *Diabetologia*,(1987) 29: pp. 63-67

Low Concentrations of Interleukin - 1 Stimulate and High Concentrations Inhibit Insulin Release from Isolated Rat Islets of Langerhans, Giatgen A. Spinas, et al., *ACTA Endocrinologica (Copenh)* (1986), 113: pp.551-558

Mouse Islet Cell Lysis Mediated by Interleukin-1-Induced Fas, K. Yamada, et al., *Diabetologia* (1996) 39: pp.1306-1312

Interleukin-1B-Induced Formation of EPR-Detectable Iron-Nitrosyl Complexes in Islets of Langerhans, John A. Corbett, et al., *The Journal of Biological Chemistry*, Vol. 266, No. 32, pp. 21351-21354

Adenoviral Gene Transfer of the Interleukin-1 Receptor Antagonist Protein To Human Islets Prevents IL-1B-Induced B-Cell Impairment and Activation of Islet Cell Apoptosis In Vitro, Nich Giannoukakis, et al., *Diabetes*, Vol. 48, September 1999, pp. 1730-1736

Prevention of Beta Cell Dysfunction and Apoptosis Activation in Human Islets by Adrenoviral Gene Transfer of the Insulin-Like Growth Factor, N. Giannoukakis, et al., *Gene Therapy* (2000) 7, pp.2015-2022

Human Islets of Langerhans Express Fas Ligand and Undergo Apoptosis in Response to Interleukin-1B and Fas Ligation, Anne C. Loweth, et al., *Diabetes*, Vol. 47, May 1998, pp. 727-732

Cytotoxic Effects of of Cytokines on Human Pancreatic Islet Cells in Monolayer Culture, Alexander Rabinovitch, et al., *Journal of Clinical Endocrinology and Metabolism*, Vol. 71, No. 1, pp.152-156

EXAMINER

/Ian Dang/

DATE CONSIDERED

03/27/2007



AUG 22 2005

Examiner: Ian Dang Art Unit 1647

Sheet 3 of 5 (08/18/05)

|        |  |
|--------|--|
| /I.D./ | Nitric Oxide Primes Pancreatic B Cells for Fas-Mediated Destruction in Insulin-Dependant Diabetes Mellitus, Giorgio Stassi, et al., <i>J. Exp. Med.</i> , Vol. 186, Number 8, October 20, 1997, pp. 1193-1200                              |
|        | Interleukin-1B-Induced Nitric Oxide Synthase Expression by Rat Pancreatic B-Cells: Evidence for the Involvement of Nuclear Factor kB in the Signaling Mechanism, Guim Kwon, et al., <i>Endocrinology</i> , Vol. 136, No. 11, pp. 4790-4795 |
|        | Cytokine Induction of Fas Gene Expression in Insulin-Producing Cells Requires the Transcription Factors NF-kB and C/EBP, Martine I. Darville, et al., <i>Diabetes</i> , Vol. 50, pp 1741-1748  |
|        | Cytokines Activate the Nuclear Factor kB (NF-kB) and Induce Nitric Oxide Production in Human Pancreatic Islets, Malin Flodström, et al., <i>Federation of European Biochemical Societies</i> , 385, (1996) pp. 4-6                         |
|        | Improved Human Islet Isolation Using a New Enzyme Blend, Liberase, Elina Linetsky, et al., <i>Diabetes</i> , Vol. 46, July 1997, pp. 1120-1123   |
|        | Human Islet Transplantation, José Oberholzer, et al., <i>Transplantation</i> , Vol. 69, No. 6, March 27, 2000, pp. 1115-1123   |
|        | Automated Method for Isolation of Human Pancreatic Islets, Camillo Ricordi, et al., <i>Diabetes</i> , Vol. 37, April 1988, pp. 413-420   |
|        | Monolayer Culture of Adult Rat Pancreatic Islets on Extracellular Matrix: Modulation of B-Cell Function by Chronic Exposure to High Glucose, Nurit Kaiser, et al., <i>Endocrinology</i> , Vol. 129, No. 4, pp. 2067-2076                   |
|        | Apoptosis-Inducing Membrane Vesicles, Satoshi Jodo, et al., <i>The Journal of Biological Chemistry</i> , Vol. 276, No. 43, Issue of October 26, 2001, pp. 39938-39944  |
|        | Nitric Oxide Synthase Is Not a Constituent of the Antimicrobial Armature of Human Mononuclear Phagocytes, Markus Schneemann, et al., <i>The Journal of Infectious Diseases</i> , 1993, 167, pp. 1358-1363                                  |
|        | Identification of Programmed Cell Death In Situ via Specific Labeling of Nuclear DNA Fragmentation, Yael Gavrieli, et al., <i>The Journal of Cell Biology</i> , Vol. 119, Number 3, November 1992 pp. 493-501                              |
|        | N-Terminal DNA-Binding Domains Contribute to Differential DNA-Binding Specificities of NF-kB p50 and p65, Michel B. Toledo, et al., <i>Molecular and Cellular Biology</i> , Feb. 1993, Vol. 13, No. 2, pp. 852-860                         |
|        | How NF-kB is Activated: The Role of the I kB Kinase (IKK) Complex, Michael Karin, <i>Oncogene</i> , (1999) 18: pp.6867-6874  |
|        | B-Cell Death During Progression to Diabetes, Diane Mathis, et al., <i>Nature</i> , Vol 414, Dec. 2001 pp. 792-798  |
|        | Evidence of Islet Cell Autoimmunity in Elderly Patients with Type 2 Diabetes, Massimo Pietro, et al., <i>Diabetes</i> , Vol. 49, Jan. 2000, pp. 32-38  |
|        | Antibodies to Glutamic Acid Decarboxylase Discriminate Major Types of Diabetes Mellitus, Merrill J. Rowley, et al., <i>Diabetes</i> , Vol. 41, April 1992, pp. 548-551   |
|        | The Accelerator Hypothesis: Weight Gain as the Missing Link Between Type I and Type II Diabetes, T. J. Wilkin, <i>Diabetologia</i> (2001) 44:pp 914-922  |
|        | Processing of Engulfed Apoptotic Bodies Yields T Cell Epitopes, Matteo Bellone, et al., <i>The Journal of Immunology</i> 1997, 159:pp. 5391-5399   |
|        | Perspectives in Diabetes Neonatal B-Cell Apoptosis, A Trigger for Autoimmune Diabetes?, Jacqueline D. Trudeau, et al., <i>Diabetes</i> , Vol. 49, January 2000 pp. 1-7   |
|        | Activation of Intraislet Lymphoid Cells Causes Destruction of Islet Cells, Paul E. Lacy, et al., <i>American Journal of Pathology</i> , Vol. 138, No. 5, May 1991, pp. 1183-1190   |
|        | The Intraislet Macrophage and Type I Diabetes, Paul E. Lacy M.D., <i>The Mount Sinai Journal of Medicine</i> , Vol. 61, No. 2, March 1994, pp. 170-174   |
|        | Potential Role of Resident Islet Macrophage Activation in the Initiation of Autoimmune Diabetes, Marc Arnush, et al., <i>The Journal of Immunology</i> , 1998, 160: pp.2684-2691   |
| ▼      | Pancreatic B-Cell Damage Mediated by B-Cell Production of Interleukin-1, Monique R. Heitmeier, et al., <i>The Journal of Biological Chemistry</i> , Vol. 276, No. 14, April 6, 2001, pp. 11151-11158                                       |

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|-------|--|
| I.D./ | Hyperinsulinemia and Glucagon Deficiency in the Diabetic Psammomys obesus, M. Gakot, et al., <i>Endocrinology</i> , May 20, 2005, Vol. 135, No. 5.   |
|       | Monocytic Chemoattractant Protein-1 is Expressed in Pancreatic Islets from Prediabetic NOD Mice and In Interleukin-1B-exposed Human and Rat Islet Cells, M.-C Chen, et al., <i>Diabetologia</i> (2001) 44: pp. 325-332                               |
|       | B-Cell Apoptosis and Defense Mechanisms, Lessons from Type 1 Diabetes, Decio L. Elizirik, et al., <i>Diabetes</i> , Vol. 50, Suppl. 1, Feb. 2001, pp. S64-S69  |
|       | Cytokines Induce Apoptosis in B-Cells Isolated From Mice Lacking the Inducible Isoform of Nitric Oxide Synthase (iNOS-/-), Dongbo Liu, et al., <i>Diabetes</i> , Vol. 49, July 2000, pp. 1116-2000   |
|       | Nitric Oxide Production and Fas Surface Expression Mediate Two Independent Pathways of Cytokine-Induced Murine B-Cell Damage, Urs Zumsteg, et al., <i>Diabetes</i> , Vol. 49, Jan. 2000, pp. 39-47   |
|       | Protection of Human Islets from the Effects of Interleukin-1B by Adenoviral Gene Transfer of an IκB Repressor, Nicholas Giannoukakis, et al., <i>The Journal of Biological Chemistry</i> , Vol. 275, No. 47, Issue of Nov. 24, 2000, pp. 36509-36513 |
|       | Nitric Oxide Mediates Cytokine-Induced Inhibition of Insulin Secretion by Human Islets of Langerhans, John A. Corbett, et al., <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 90 pp. 1731-1735, March 1993 Medical Sciences                                |
|       | Hyperglycemia-Induced Activation of Nuclear Transcription Factor κB in Vascular Smooth Muscle Cells, Kiran Kumar, et al., <i>Diabetes</i> , Vol. 48, April 1999, pp. 855-864   |
|       | Inhibition of Cytokine-Induced NF-κB Activation by Adenovirus-Mediated Expression of a NF-κB Super-Repressor Prevents B-Cell Apoptosis, Harry Heimberg, et al., <i>Diabetes</i> , Vol. 50, Oct. 2001, pp. 2219-2224                                  |
|       | Imidazoline Compounds Protect Against Interleukin 1B-Induced B-Cell Apoptosis, Sergei V. Zaitsev, et al., <i>Diabetes</i> , Vol. 50, Suppl. 1, Feb. 2001, pp. S70-S76  |
|       | Improved Beta-Cell Function after Intensive Insulin Treatment in Severe Non-Insulin-Dependent Diabetes, Benjamin Glaser, et al., <i>ACTA Endocrinologica (Copenh)</i> 1988, 118: pp. 365-373   |
|       | B-Cell Deficit and Increased B-Cell Apoptosis in Humans With Type 2 Diabetes, Alexandra E. Butler, et al., <i>Diabetes</i> , Vol. 52, January 2003, pp. 102-110  |
|       | Early Differential Defects of Insulin Secretion and Action in 19-Year-Old Caucasian Men Who Had Low Birth Weight, Christine B. Jensen, et al., <i>Diabetes</i> , Vol. 51, April 2002, pp. 1271-1280  |
|       | Age-Dependent Impact of Zygosity and Birth Weight on Insulin Secretion and Insulin Action in Twins, P. Poulsen, et al., <i>Diabetologia</i> (2002), pp. 1649-1657  |
|       | Metabolic Impact of a Family History of Type 2 Diabetes. Results from a European Multicentre Study (EGIR), A. Vaag, et al., 2001 <i>Diabetes UK. Diabetic Medicine</i> , 18, pp. 553-540   |
|       | Journal Symposium, Islet Growth and Development in the Adult, S. Bonner-Weir, <i>Journal of Molecular Endocrinology</i> (2000) 24, pp. 297-302   |
|       | Islet Pathology and the Pathogenesis of Type 1 and Type 2 Diabetes Mellitus Revisited, Günter Klöppel, et al., <i>Surv. Synth. Path. Res.</i> 4: pp. 110-125 (1985)  |
|       | Reduced Beta-Cell Mass and Expression of Oxidative Stress-Related DNA Damage in the Islet of Japanese Type II Diabetic Patients, H. Sakuraba, et al., <i>Diabetologia</i> (2002) 45: pp. 85-96   |
|       | Selective B-Cell Loss and α-Cell Expansion in Patients with Type 2 Diabetes Mellitus in Korea, Kun Ho Yoon, et al., <i>The Journal of Clinical Endocrinology &amp; Metabolism</i> 88(5), pp. 2300-2308   |
|       | B-Cell Dysfunction and Insulin Resistance in Type 2 Diabetes: Role of Metabolic and Genetic Abnormalities, Derek LeRoith, M.D., Ph.D., FACP, <i>The American Journal of Medicine</i> , Vol. 113(6A), pp. 3S-11S                                      |
|       | Fatty Acids, Lipotoxicity and Insulin Secretion, J.D. McGarry, et al., <i>Diabetologia</i> (1999) 42: pp. 128-138  |
|       | The Glucose Fatty Acid Cycle in Obesity and Maturity Onset Diabetes Mellitus, P. J. Randle, et al., <i>Annals New York Academy of Sciences</i> , pp. 324-333   |
| ▼     | Lipotoxicity in the Pathogenesis of Obesity-Dependent NIDDM, Genetic and Clinical Implications, Roger H. Unger, <i>Diabetes</i> , Vol. 44, Aug. 1995, pp. 863-870  |

EXAMINER

Ian Dang/

DATE CONSIDERED

03/27/2007

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Examiner: Ian Dang Art Unit 1647

Sheet 5 of 5 (08/18/05)

|          |  |
|----------|--|
| I.D./    | Monounsaturated Fatty Acids Prevent the deleterious effects of Palmitate and High Glucose on Human Pancreatic B-Cell Tumors and Function, Kathrin Maedler, et al., <i>Diabetes</i> , Vol. 52, March 2003, pp. 726-733      |
|          | Glucose-Induced B Cell Production of IL-1B Contributes to Glucotoxicity in Human Pancreatic Islets, Kathrin Maedler, et al., <i>The Journal of Clinical Investigation</i> , Sept. 2002, Vol. 110, Number 6, pp. 851-860    |
|          | FLIP Switches FAS-Mediated Glucose Signaling in Human Pancreatic B Cells From Apoptosis to Cell Replication, Kathrin Maedler, et al., <i>PNAS</i> , June 11, 2002, Vol. 99, No. 12, pp. 8236-8241                          |
|          | Islet Secretion in a New Experimental Model for Non-Insulin-Dependent Diabetes, G. C. Weir, et al., <i>Diabetes</i> , Vol. 30, July 1981, pp. 590-595  |
|          | Partial Pancreatectomy in the Rat and Subsequent Defect in Glucose-Induced Insulin Release, S. Bonner-Weir, <i>J. Clin. Invest.</i> , Vol. 71, June 1983, pp. 1544-1554  |
|          | Hyperglycaemia as an inducer as well as a consequence of Impaired Islet Cell Function and Insulin Resistance: Implications for the management of diabetes, R. H. Under, et al., <i>Diabetologia</i> (1985) 28: pp. 119-121 |
|          | Positional Cloning of the Mouse Obese Gene and its Human Homologue, Yiyi Zhang, et al., <i>Nature</i> , Vol. 372, Dec. 1994, pp. 425-432   |
|          | Recombinant Mouse OB Protein: Evidence for a Peripheral Signal Linking Adiposity and Central Neural Networks, L. Arthur Campfield, et al., <i>Science</i> , Vol. 269, July 28, 1995, pp. 546-549                           |
|          | Expression of the Functional Leptin Receptor mRNA in Pancreatic Islets, Valur Emilsson, et al., <i>Diabetes</i> , Vol. 46, Feb. 1997, pp. 313-316  |
|          | Leptin Receptors Expressed on Pancreatic B-Cells, T. Kieffer, et al., <i>Biochemical and Biophysical Research Communications</i> 224, pp. 522-527 (1996), Art. 1059  |
|          | Inhibition of Glucose-Induced Insulin Secretion by Long-Term Preexposure of Pancreatic Islets to Leptin, R. Roduit, et al., <i>FEBS Letters</i> 415 (1997) pp. 179-182   |
|          | Fetal Pancreatic Islets Express Functional Leptin Receptors and Leptin Stimulates Proliferation of Fetal Islet Cells, MS Islam, et al., <i>International Journal of Obesity</i> (2000) 24, pp. 1246-1253                   |
|          | Leptin Increases the Viability of Isolated Rat Pancreatic Islets by Suppressing Apoptosis, S. Okuya, et al., <i>Endocrinology</i> , 142, (11) 4827-4830  |
|          | Protection Against Lipoapoptosis of B Cells Through Leptin-Dependent Maintenance of Bcl-2 Expression, M. Shimabukuro, et al., <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 95, pp. 9558-9561                                   |
|          | Leptin Induces Proliferation of Pancreatic B Cell Line MIN6 through Activation of Mitogen-Activated Protein Kinase, K. Tanabe, et al., <i>Biochemical and Biophysical Research Communications</i> , 241: pp. 765-768(1997) |
|          | A Urine Inhibitor of Interleukin 1 Activity Affects Both Interleukin 1a and 1b But Not Tumor Necrosis Factor, P. Seckinger, et al., <i>The Journal of Immunology</i> , Vol. 139, 1541-1545, No. 5, Sept. 1, 1987           |
|          | A Urine Inhibitor of Interleukin 1 Activity That Blocks Ligand Binding, P. Seckinger, et al., <i>The Journal of Immunology</i> , Vol. 139, 1546-1549   |
|          | Biological Role of Interleukin 1 Receptor Antagonist Isoforms, W. Arend, et al., <i>Am Rheum Dis</i> 2000;59(suppl 1) i60-i64  |
|          | Leptin Directly Induces the Secretion of Interleukin 1 Receptor Antagonist in Human Monocytes, C. Gabay, et al., <i>The Journal of Clinical Endocrinology and Metabolism</i> , Vol. 86, NO.2, pp. 783-791                  |
|          | Inflammatory Mediators and Islet B-Cell Failure: A Link Between Type 1 and Type 2 Diabetes, M. Donath, et al., <i>J. Mol. Med.</i> (2003) 81: 455-470  |
|          | Non-Insulin Dependent Diabetes Mellitus..., K. Polonsky M.D., et al., <i>Seminars in Medicine of the Beth Israel Hospital</i> , Boston, Vol. 334, No. 12, pp. 777-783  |
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